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Different effects of ATP on the contractile activity of mice diaphragmatic and skeletal muscles

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Abstract

Apart from acetyl-choline (Ach), adenosine-5′-trisphosphate (ATP) is thought to play a role in neuromuscular function, however little information is available on its cellular physiology. As such, effects of ATP and adenosine on contractility of mice diaphragmatic and skeletal muscles (m. extensor digitorum longa—MEDL) have been investigated in *in vitro* experiments. Application of carbacholine (CCh) *in vitro* in different concentrations led to pronounced muscle contractions, varying from 9.15 ± 4.76 to 513.13 ± 15.4 mg and from 44.65 ± 5.01 to 101.46 ± 9.11 mg for diaphragm and MEDL, respectively. Two hundred micromolars of CCh in both muscles caused the contraction with the 65% (diaphragm) to 75% (MEDL) of maximal contraction force—this concentration was thus used in further experiments. It was found that application of ATP (100 μM) increased the force of diaphragmatic contraction caused by CCh (200 μM) from 335.2 ± 51.4 mg ($n = 21$) in controls to 426.5 ± 47.8 mg ($n = 10$; $P < 0.05$), but decreased the contractions of MEDL of CCh from 76.6 ± 6.5 mg ($n = 26$) in control to 40.2 ± 9.0 mg ($n = 8$; $P < 0.05$). Application of adenosine (100 μM) had no effect on CCh-induced contractions of these muscles.

Resting membrane potential (MP) measurements using sharp electrodes were done at 10, 20 and 30 min after the application of ATP and adenosine. Diaphragm showed depolarization from 75 ± 0.6 down to 63.2 ± 1.05, 57.2 ± 0.96 and 53.6 ± 1.1 mV after 10, 20 and 30 min of exposition, respectively (20 fibers from 4 muscles each, $P < 0.05$ in all three cases). Adenosine showed no effect on diaphragmatic MP. Both agents were ineffective in case of MEDL.

The effects of ATP in both tissues were abolished by suramin (100 μM), a P2-receptor antagonist, and chelerythrin (50 μM), a specific protein-kinase C (PKC) inhibitor, but were not affected by 1*H*-[1,2,4]-oxadiazolo-[4,3-α]-quinoxalin-1-one (ODQ, 1 μM), a guanylyl-cyclase inhibitor, or by adenosine-3,5-monophosphothioate (Rp-cAMP, 1 μM), a protein-kinase A (PKA) inhibitor.

Besides the action on contractile activity, ATP (100 μM) led to a significant ($P < 0.001$) depolarization of diaphragm muscle fibers from 74.5 ± 2.3 down to 64 ± 2.1, 58.2 ± 2.2 and 54.3 ± 2.4 mV after 10, 20 and 30 min of incubation, respectively. Incubation of MEDL with the same ATP concentration showed no significant change of MP.

Denervation of the muscles for 28 days led to a decrease of CCh-induced contractions of diaphragm down to 171.1 ± 34.5 mg ($n = 11$, $P < 0.05$), but increased the contractile force of MEDL up to 723.9 ± 82.3 mg ($n = 9$, $P < 0.01$). Application of ATP elevated the contractility of denervated diaphragm caused by CCh up to normal values (311.1 ± 79.7 mg, $n = 6$, $P > 0.05$ versus control), but did not significantly affect of contractility of MEDL, which became 848.1 ± 62.7 mg ($n = 6$).

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